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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,973	STANTON ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1, 2 and 4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/6/2006. Claims 1-9 are pending. An office action on the merits of claims 3 and 5-9 follows.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 3 and 5-9 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]
"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the specific and substantial tests (see below).

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example,

both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. ' 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility."

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a specific or substantial utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial asserted utility would be considered to be met.

A "Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.
See also the MPEP at 2107 - 2107.02.

The claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid. The specification teaches that the invention is based on the identification of a gene that is differentially expressed in the left ventricle of the rat Myocardial infarction model, in the rat Cardiac Hypertrophy Model, and in the mouse Viral Myocarditis model (p. 20, lines 9-11). Claim 3 is directed to an array which comprises any oligonucleotide which is complementary to a “reference” RNA or DNA encoding SEQ ID NO: 1 or a mammalian homologue thereof,

wherein the reference DNA or RNA is obtained from both a biological sample taken from a normal subject and a biological sample taken from a subject exhibiting a cardiac, renal of inflammatory disease or from a biological sample taken at different stages of a cardiac, renal or inflammatory disease. The specification asserts that the nucleic acids of the invention, and particularly SEQ ID NO 2 can be used to design specific probes and primers, can be used in detection, diagnostic, prognostic methods, vector constructs, antibody constructs, etc (p. 42-48). However, these are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acid being claimed.

Further, the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The specification states that when characterization of the differentially expressed genes indicate that modulation of the gene's expression or the gene product's activity can inhibit or treat a disease, specifically cardiac, kidney, or inflammatory diseases, the differentially expressed gene or it's gene product becomes a potential drug candidate or a target for developing a drug candidate for the treatment of a cardiac, kidney or inflammatory disease, or may be used as a diagnostic. However, the specification has not taught the activity of the polypeptide of SEQ ID NO: 1, or a mammalian homologue thereof, nor has the specification demonstrated that the modulation of the expression of a nucleic acid encoding such polypeptide can be used to inhibit or treat any kidney, inflammatory, or cardiac disease, including viral myocarditis, cardiac hypertrophy, or myocardial infarction. The need for such research clearly indicates that the nucleic acid or the protein it encodes is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those

instances where the final product is not supported by a specific and substantial utility. Further, a starting material does not have substantial utility when further experimentation must be conducted to determine the use for that starting material. The research contemplated by applicant(s) to characterize potential protein products, and determine therapeutic and diagnostic uses does not constitute a specific and substantial utility. Identifying and studying the properties of a nucleic acid or protein itself or the mechanisms in which such are involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

The specification teaches that a differentially expressed rat sequence, termed "P00188_D12" was identified by analysis of left ventricle tissue obtained from an in vivo model of ventral myocarditis (page 56). The specification asserts that the differentially expressed nucleic acids can be used as a diagnostic. This assertion has been thoroughly reviewed, however the teachings of the specification do not support how one of skill in the art would use the claimed nucleic acid as a diagnostic. Firstly, it is noted that the specification teaches that in vivo experimentation revealed that in the rat myocardial infarction model and the rat cardiac hypertrophy model, the gene corresponding to SEQ ID NO 2 was under expressed by about 1.8 fold and 2.5 fold, respectively. This expression pattern, however, does not appear to diagnostic

of cardiac diseases in general as the specification teaches that in vivo, the gene corresponding to SEQ ID NO 2 was over expressed in the mouse viral myocarditis model (See p. 65, lines 15-24). Furthermore, the specification fails to teach corroborative evidence for such *in vivo* expression patterns. The specification teaches that in *in vitro* experiments, rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy (see p. 72, lines 7-9). However, while SEQ ID NO 2 was under expressed in the in vivo rat cardiac hypertrophy model, it was over expressed in cardiac myocytes cells where cardiac hypertrophy was induced (see p. 74, and figure 4). Therefore, given the results in the specification, the skilled artisan would not be able to identify any specific cardiac disease based on detection of either over expression or under expression of SEQ ID NO 2. Further experimentation would be required of the skilled artisan to reasonably confirm a real world context of use for the claimed nucleic acids.

At page 66, the specification teaches that the putative protein (SEQ ID NO: 1) encoded by SEQ ID NO: 2 contains a putative signal sequence and a "probable" transmembrane region. However, a large number of proteins with different functions contain both of these types of domains, such that the possession of these domains does not convey to the skilled artisan any specific or substantial utility for the claimed sequences. Additionally, the specification teaches that a BLAST search revealed "a good match" for SEQ ID NO: 2 with 3 different ESTs, however the specification does not teach the degree of homology present, nor the function of these ESTs. Additionally, even if the function were known, such evidence would not predictably establish the function of the polypeptide of SEQ ID NO: 1. Fetrow teaches (Fetrow et al., J. Mol. Biol., vol. 282, pp 703-711, 1998) that although function prediction by homology to previously

characterized proteins is extremely successful and is fast, cheap and reliable, there are several problems that limit its potential utility, one of which is that sequence homology does not guarantee functional similarity (p 704, col. 1, 1st full paragraph). Fetrow teaches that "threading"(analysis using structure prediction tools) can identify topological cousins, that is , protein families such as the α/β barrels with similar structures, but dissimilar functions. Fetrow teaches using a three dimensional descriptor of the active site of a protein, termed "fuzzy functional form" (FFF) and argues that threading alone is not enough to provide the required information about function because it has been shown that pairs of proteins can have similar structures but unrelated functions (p. 706, col. 2, last para). Fetrow teaches that because such topological cousins exist, knowledge of the structure is not equivalent to identification of protein function. Skolnick (Skolnick and Fetrow, TIBTECH, January 2000, vol. 18, pp 34-39) teaches (p. 35, "Box 1") that a common protein characteristic that makes functional analysis based only on homology especially difficult is the tendency of proteins to be multifunctional. Skolnick teaches that for example, lactate dehydrogenase binds NAD, substrate, and zinc and performs a redox reaction and that each of these occurs at different functional sites that are in close proximity and the combination of all four sites creates the fully functional proteins. Skolnick also cites RecA which contains a DNA binding domain, a multimerization domain and additional sites that bind regulatory proteins. Skolnick also teaches that the serine threonine phosphatase superfamily is a prime example of the difficulties of using standard sequence analysis to recognize the multiple functions found in single proteins. Skolnick teaches that this large protein family is divided into a number of subfamilies, all of which contain an essential phosphatase active site. He teaches that subfamilies 1, 2A and 2b exhibit 40% or more sequence identity

between them, however each of these subfamilies is apparently regulated differently by the cell and observation suggest that there are different functional sites at which regulation can occur. Skolnick teaches that because the sequence identity between subfamilies is so high, standard sequence similarity methods could easily misclassify new sequences as members of the wrong subfamily if the functional sites are not carefully considered.

As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3, and 5-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making an array comprising a nucleic acid molecule encoding the protein of SEQ ID NO: 1 or the complement of the nucleic acid molecule, does not reasonably provide enablement for an array comprising one or more oligonucleotides complementary to reference RNA or DNA encoding a protein of SEQ ID NO: 1 or mammalian homologue thereof, wherein the reference DNA or RNA are obtained as indicated in claim 3, or a diagnostic kit for the detection of a cardiac, kidney, or inflammatory disease comprising an array of claim 3, or an antibody to a mammalian homolog of a polypeptide of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make or use the invention commensurate in scope with these claims, or to a method of using an array comprising a nucleic acid molecule encoding the protein of SEQ ID NO: 1 or the complement of the nucleic acid molecule. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, including an array comprising a nucleic acid molecule encoding the protein of SEQ ID NO: 1, or the complement of the nucleic acid molecule.

With regard to methods of making the claimed nucleic acids and antibodies, it is noted that the invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)). The claims are broadly drawn to an array and kit comprising one or more oligonucleotides complementary to a "reference" RNA or DNA encoding a protein of SEQ ID NO: 1 or another mammalian homologue thereof, wherein the

reference DNA or RNA sequences are obtained from both a biological sample taken from a normal subject and a biological sample taken from a subject exhibiting a cardiac, renal of inflammatory disease or from a biological sample taken at different stages of a cardiac, renal or inflammatory disease. The kits are asserted to be diagnostic for a cardiac, kidney, or inflammatory disease; however the specification does not teach any diagnostic for detecting the extremely broad range of disease encompassed by the claims. The specification does not define the term "reference". Additionally, the term "complementary" refers to the ability of sequences to hybridize to each other by hydrogen bonding. A sequence need not be completely complementary to another sequence to hybridize to it. Accordingly, the claims are not limited to sequences which are completely complementary to SEQ ID NO: 2 (encodes SEQ ID NO: 1), but more broadly encompass variants, and homologues from any mammalian source, as well as genomic sequences which have not been taught in the specification. Additionally, the claims are specifically drawn to nucleic acids which encode any mammalian homologue of SEQ ID NO: 1 or an antibody to such a homologue. However, the specification does not teach the function of SEQ ID NO: 1, nor any mammalian homologues thereof. Accordingly, the specification provides no guidance to the skilled artisan to be able to predictably determine whether a sequence is a homologue of SEQ ID NO: 1, other than by SEQ ID NO:.

The specification teaches that a differentially expressed rat sequence, termed "P00188_D12" was identified by analysis of left ventricle tissue obtained from an in vivo model of ventral myocarditis (page 56). The specification asserts that the differentially expressed nucleic acids can be used as a diagnostic. This assertion has been thoroughly reviewed, however the teachings of the specification do not provide any guidance to the skilled artisan to make

broadly "any" nucleic aid molecule complementary to any reference RNA or DNA encoding SEQ ID NO: 1, isolated from different types of samples set forth in claim 3 to be used as a diagnostic not do the teachings of the specification support how one of skill in the art would use the claimed nucleic acid as a diagnostic. Firstly, it is noted that the specification teaches that in vivo experimentation revealed that in the rat myocardial infarction model and the rat cardiac hypertrophy model, the gene corresponding to SEQ ID NO 2 was under expressed by about 1.8 fold and 2.5 fold, respectively. This expression pattern, however, does not appear to diagnostic of cardiac diseases in general as the specification teaches that in vivo, the gene corresponding to SEQ ID NO 2 was over expressed in the mouse viral myocarditis model (See p. 65, lines 15-24). Furthermore, the specification fails to teach corroborative evidence for such *in vivo* expression patterns. The specification teaches that in *in vitro* experiments, rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy (see p. 72, lines 7-9). However, while SEQ ID NO 2 was under expressed in the in vivo rat cardiac hypertrophy model, it was over expressed in cardiac myocytes cells where cardiac hypertrophy was induced (see p. 74, and figure 4). Therefore, given the results in the specification, the skilled artisan would not be able to identify any specific cardiac disease based on detection of either over expression or under expression of SEQ ID NO 2. Further, the specification is silent as to any renal of inflammatory disease which may be associated with SEQ ID NO: 1 or 2.

Although the level of skill in the art of microbiology is high, the level of experimentation required to make and use the claimed invention is even higher. The practice the invention as broadly as it is claimed, the skilled artisan would be required to determine the activity and function of the protein of SEQ ID NO: 1 and to screen a large number of variants and

homologues from any source to identify sequences which are a "reference" DNA or RNA encoding SEQ ID NO: 1, as well as mammalian homologues thereof. Given that neither the specification nor the art provide guidance as to the function of SEQ ID NO: 1, this experimentation would be replete with trial by error analysis, requiring a large amount of inventive effort, with many of the intervening steps not being assured of a successful result. Additionally, given the conflicting guidance in the specification regarding the very different expression patterns of nucleic acids encoding SEQ ID NO: 1 in different cardiac models, the skilled artisan would be required to perform a large amount of trial and error experimentation to arrive at a diagnostic for any oligonucleotide complementary to a nucleic acid encoding SEQ ID NO: 1, with regard to the extremely broad scope of diseases encompassed by the claims. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

6. Claims 3 and 5-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to an array and kit comprising one or more oligonucleotides complementary to a "reference" RNA or DNA encoding a protein of SEQ ID NO: 1 or another mammalian homologue thereof, wherein the reference DNA or RNA sequences are obtained from both a biological sample taken from a normal subject and a biological sample taken from a subject exhibiting a cardiac, renal of inflammatory disease or from a biological sample taken at different stages of a cardiac, renal or inflammatory disease. The kits are asserted to be diagnostic for a cardiac, kidney, or inflammatory disease, however the specification does not teach any diagnostic for detecting the extremely broad range of disease encompassed by the claims. The specification does not define the term "reference". Additionally, the term "complementary" refers to the ability of sequences to hybridize to each other by hydrogen bonding. A sequence need not be completely complementary to another sequence to hybridize to it. Accordingly, the claims are not limited to sequences which are completely complementary to SEQ ID NO: 2 (encodes SEQ ID NO: 1), but more broadly encompass variants, and homologues from any mammalian source, as well as genomic sequences which have not been taught in the specification. Additionally, the claims are specifically drawn to nucleic acids which encode any mammalian homologue of SEQ ID NO: 1 or an antibody to such a homologue. However, the specification does not teach the function of SEQ ID NO: 1, nor any mammalian or human homologue thereof. Accordingly, the specification provides no guidance to the skilled artisan to be able to predictably determine whether a sequence is a homologue of SEQ ID NO: 1, other than by SEQ ID NO:. The genus encompassed by the claims is extremely large, encompass mutants, variants and homologues of nucleic acid molecules which encode SEQ ID NO: 1, from any source. However, the specification does not define the attributes or features of the members

of the genus, such that the skilled artisan would not be able to determine which sequences belonged to the genus. The specification does not provide any guidance regarding any specific attributes or features which would be characteristic, identifying a sequence as another mammalian homologue, or more specifically, a human sequence. The single species of SEQ ID NO: 2 is not representative of the large genus of possible sequences encompassed by the broad claims because one of skill in the art would not be able to envision, given the sequence of SEQ ID NO: 1 or 2, the members of the genus encompassed by the broadly claimed invention.

For example, the following "human" sequence may be considered a homologue of SEQ ID NO: 1, however it is not taught or described by the specification.

```
DEFINITION  Homo sapiens high density lipoprotein-binding protein (HBP1) mRNA,
            complete cds.
ACCESSION   AY245915
VERSION     AY245915.1  GI:29650884
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (bases 1 to 2281)

Alignment Scores:
Pred. No.:                1.4e-29        Length:          2281
Score:                    460.50         Matches:         100
Percent Similarity:       52.3%          Conservative:    24
Best Local Similarity:    42.2%          Mismatches:      56
Query Match:              35.6%          Indels:          57
DB:                       5              Gaps:            5

US-10-775-973-1 (1-236) x AY245915 (1-2281)

Qy          1 MetLysAlaLeuArgAlaValLeuLeuIleLeuLeuLeuSerGlyGlnProGlySerSer 20
              ||||||||||||   ||||||||||||   |||||||||   |||:::||||||
Db         76 ATGAAGGCGCTCGGGGCTGTCCTGCTTGCCCTCTTGCTGTGCGGGCGGCCAGGGAGAGGG 135

Qy         21 TrpAlaGlnGluAlaGlyAspValAspLeuGluLeuGluArgTyrSerTyrAspAspAsp 40
                    |||:::                  |||   |||             |||
Db        136 CAGACACAGCAG-----------------GAGGAAGAGGAAGAGGACGAGGACCACGGG 177

Qy         41 GlyAspAspAspAspAspAspGluGluGlu---GluGluGluGluThrAsnMetIle 59
                 ||||||   |||::::::||||||:::|||   ||||||||||||||||||   :::
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Db        178 CCAGATGACTACGACGAGGAAGATGAGGATGAGGTTGAAGAGGAGGAGACCAACAGGCTC 237

Qy         60 ProGlySerArgAspArgAlaProProLeuGlnCysTyrPheCysGlnValLeuHisSer 79
                |||||   |||   |||         |||:::||||||   |||:::   |||
Db        238 CCTGGTGGCAGGAGCAGAGTG---CTGCTGCGGTGCTACACCTGCAAGTCCCTGCCCAGG 294

Qy         80 GlyGluSerCysAsnGluThrGlnArgCysSerSerSerLysProPheCysIleThrVal 99
                |||   ||||||   ||||||   ||||||      :::      |||   |||:::
Db        295 GACGAGCGCTGCAACCTGACGCAGAACTGCTCACATGGCCAGACC---TGCACAACCCTC 351

Qy        100 IleSerHisGlyLysThrAspThrGlyValLeuThrThrTyrSerMetTrpCysThrAsp 119
                |||:::||||||   |||::::::|||:::||||||||||:::|||   ||||||||||
Db        352 ATTGCCCACGGGAACACCGAGTCAGGCCTCCTGACCACCCACTCCACGTGGTGCACAGAC 411

Qy        120 ThrCysGlnProIleValLysThrValAspSerThrGlnMetThrGlnThrCysCysGln 139
                :::||||||||||||   |||||||||:::   ||||||:::|||   ||||||||||
Db        412 AGCTGCCAGCCCATCACCAAGACGGTGGAGGGGACCCAGGTGACCATGACCTGCTGCCAG 471

Qy        140 SerThrLeuCysAsnIleProProTrpGlnSerProGlnIleHisAsnProLeuGlyGly 159
                |||:::|||||||||:::|||||||||||||||   ::::::   :::
Db        472 TCCAGCCTGTGCAATGTCCCACCCTGGCAAAGCTCCCGAGTCCAGGAC---------- 519

Qy        160 ArgAlaAspSerProLeuLysGlyGlyThrArgHisProGlnGlyAspArgPheSerHis 179

Db        519 ---------------------------------------------------------- 519

Qy        180 ProGlnValValLysValThrHisProGlnSerAspGlyAlaHisLeuSerLysGlyGly 199

Db        519 ---------------------------------------------------------- 519

Qy        200 LysAlaAsnGlnProGlnGlyAsnGlyAlaGlyPheProAlaGlyTrpSerLysPheGly 219
                        |||   |||   |||||||||   |||   |||   |||:::
Db        520 ----------CCAACAGGCAAGGGGGCAGGCGGCCCCCGGGGCAGCTCCGAAACTGTG 567

Qy        220 AsnValValLeuLeuLeuThrPheLeuThrSerLeuTrpAlaSerGlyAla 236
                      |||||||||       |||       |||   |||   ||||||
Db        568 GGCGCAGCCCTCCTGCTCAACCTCCTTGCCGGCCTTGGAGCAATGGGGGCC 618
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Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 1, 2, and a nucleic acid encoding SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 3 and 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite in the recitation of "reference" RNA or DNA as it is unclear if the term is limited to a sequence which encodes SEQ ID NO: 1 or a homologue thereof, or if it includes sequences which encode variants of either. The specification does not define the term and the metes and bounds of the claims are unclear.

Claim 3 is indefinite in the recitation of (e.g. human) as it is unclear if the use of parenthesis as well as the recitation of "e.g." (for example) are meant to limit the claim to the recitation which follows, that is "human", or not.

Claim 6(e) is indefinite in the recitation of "further mammalian homologue, as it is unclear if the claim refers to a single mammalian homologue or more than one.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 3, 5, and 6 rejected under 35 U.S.C. 102(e) as being anticipated by Fodor (Fodor et al; (US Pregrant Publication 2001/0053519, 3/6/2000).

Fodor teaches an array comprising every 10 oligonucleotide (see Example 2). The instantly claimed invention is directed to an array comprising one or more oligomers which are complementary to a large genus of possible nucleotide sequences including degenerate variants which would encode SEQ ID NO: 1 or a mammalian homologue. The claims are not limited to any particular length limitation for the oligonucleotide, nor are the claims limited to sequences which are completely complementary to the recited reference RNA or DNA. Accordingly, the claims have been given their broadest reasonable interpretation to encompass the array comprising 10 mers taught by Fodor. With respect to claim 5, the use for the kit has been given no patentable weight. Additionally, the claim adds no structural limitations that distinguish over the array of Fodor. With regard to claim 6, one of the 10 mer oligonucleotides taught by Fodor anticipates a primer, a probe, and a PCR reagent recited in claim 6.

11. Claims 3, 5, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796).

Brennan teaches making an array of all possible 10 mer nucleic acids (see cols 9 and 10). The instantly claimed invention is directed to an array comprising one or more oligomers which are complementary to a large genus of possible nucleotide sequences including degenerate variants which would encode SEQ ID NO: 1 or a mammalian homologue. The claims are not limited to any particular length limitation for the oligonucleotide, nor are the claims limited to sequences which are completely complementary to the recited reference RNA or DNA. Accordingly, the claims have been given their broadest reasonable interpretation to encompass

the array comprising 10 mers taught by Brennan. With respect to claim 5, the use for the kit has been given no patentable weight. Additionally, the claim adds no structural limitations that distinguish over the array of Brennan. With regard to claim 6, one of the 10 mer oligonucleotides taught by Brennan anticipates a primer, a probe, and a PCR reagent recited in claim 6.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Jehanne Sitton
Primary Examiner
Art Unit 1634

12/26/06